SEASONAL CHANGES IN HUMAN BODY FLUIDS

HISATO YOSHIMURA*
Department of Physiology (1st Division), Kyoto Prefectural University of Medicine, Kyoto

It is well-known that the blood properties change with seasons, and especially many reports in respect to change in water content have been made. For example, Kuroda (1) reported that the water content in blood increases in summer, while it decreases in winter. The fact can be explained by the view of Bazett (2), Sjostrand (3), Yoshimura and others (4) that the circulating blood volume, especially its plasma volume, increases in summer, while it decreases in winter. The first demonstration of the relationship between climate and blood volume was provided by Barcroft et al. (5) who were sailing from England to Peru across the equator. This increase of blood volume was attributed by previous authors to the increase of vascular bed which expands in hot climate by dilatation of cutaneous vessels (6).

On the other hand, Forbes, Dill and Hall (7) and recently Doupe (8) failed to confirm the findings of Barcroft. Bass and Henschel (8) expressed their opinion in their excellent review on climatic changes of body fluids that the lack of general agreement regarding seasonal variations in body fluids is not surprising in view of the confounding variables in these investigations.

Recently, the author (4) pointed out influencial effects of seasonal alteration of water metabolism upon body fluids which may reflect on blood volume. Little work has ever been done on the interrelation of seasonal changes in body fluid compartments with water metabolism. Moreover, the previous reports on climatic changes of body fluids are quite conflicting as was pointed out by Bass and Henshel (8), and further investigations under well controlled experimental conditions are required.

The present study was planned firstly to verify seasonal variations in amount and distribution of water and salts of body fluids in human subjects by repeating monthly measurements of body fluids at basal condition. The second aim was to observe seasonal changes of water metabolism under well controlled experimental conditions and to elucidate its possible effects upon body fluid compartments and blood properties.

METHODS

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* 吉村寿人
This paper is dedicated to Dr. Rinnosuke Shoji, Professor Emeritus of Kyoto University, in celebration of his 70th birthday.
of study mentioned in the introduction. The first series was planned to verify seasonal variations in the amount and distribution of body fluid water and salts. The subjects were 8 adult Japanese whose ages were from 24 to 42 years. They stayed in the laboratory for 3 to 4 days in the last decade of each month, and the measurements were carried out monthly at the basal condition after awaking in the morning. The blood was drawn from the cubital vein and, the specific gravity of whole blood \( G_B \) and of serum from it \( G_S \) were measured by the copper sulphate method. The hematocrit \( Ht \) and the serum water content \( Sw \) were calculated from these values by the following formulas.

\[
Ht\% = 100 \frac{(G_B - G_S)}{(1.0970 - G_S)} \quad \text{(Van Slyke et al. (9))}
\]

\[
Sw\% = 100 - \frac{[386(G_S - 1.000) - 1.39]}{G_S} \quad \text{(Fukuyama et al. (10))}
\]

The serum Na and K were measured usually by Lange’s flame photometer (11), and its chloride by Schales and Schales method (12). In some measurements, the uranyl acetate method (16) and Kramer-Tisdall (13) method were also adopted respectively for Na and K determination. With 4 subjects from the eight, the serum protein was estimated by measurement of refractive index of serum with Abbé’s refractometer (13), and its freezing point depression with Beckman’s thermometer. These measurements were repeated at least two days.

To measure the circulating serum volume, the congo red method was adopted instead of the familiar Evans blue method, because Evans blue used was readily adsorbed by the serum protein and unreasonably high values were obtained. 1\% congo red solution (10 cc.) was injected intravenously after taking the control blood sample. 4 minutes after injection, the second sample was drawn, and the color of congo red in the serum was measured with Pulfrich’s spectrophotometer, by comparing the colour with the control. The circulating serum volume was calculated from congo red concentration thus measured according to the ordinary principle of dye dilution method (13).

After the measurements of blood, the subjects got up, discharged their morning urine and the body weights were measured accurately. Four of the eight subjects lay down again in their beds and the total body water was measured by the antipyrine method (15) and the extracellular fluid volume by the rhodan method (14). In the measurement, 50 cc. of 2\% antipyrine was mixed with 20 cc. of 5\% NaSCN, and the mixture was injected slowly into the cubital vein, after the control blood sample was taken. The blood and the urine were again taken 1 hour after the injection and the concentration of rhodan was measured according to Gregerson et al. (14) with Pulfrich’s photometer. The blood was further drawn with 1 hour interval until 5 hours after the injection and the antipyrine concentration in the serum was determined according to Brodie et al. (15) with Beckman’s spectrophotometer. The rhodan space was calculated by the following equation from the quantity of rhodan injected \( T \), its amount excreted in urine \( U \) after 1 hour and its concentration \( P \) in 1 cc. serum water.
Rhodan space (extracellular space) = \((T - U)/(P \times 1.05)\)

1.05 is Donnan factor of SCN and \(P\) equals to \(P'/0.92\), where \(P'\) is the concentration in 1 cc. serum and 0.92 is its mean water content in g. The calculation of the total body water from the serum antipyrine was performed as was described by Brodie et al. (15).

The second series of experiment was planned to observe seasonal variation of water metabolism and to clarify its possible effects upon amount and distribution of body fluid. The subjects were four male adults who stayed at the laboratory for about a week in the last month of each of four seasons, i.e. February (winter), May (spring), August (summer) and November (autumn). The quantity and quality of the diet were maintained constant throughout the experiments. Its caloric content was 2,400 Cal/day and the protein content 75 g/day, with the salt seasoning of about 15 g/day. The water was taken freely by the subjects.

To determine the daily water intake by the subject, the weights of water drinks and of foods were measured daily. The same foods in quantity and quality which were taken by the subjects were reprepared for the measurements of their water contents. The foods taken in the day were mixed altogether and dried for several days by a heat dryer. The water content of the food was estimated by subtracting the weight of the dried mixture from its original weight actually eaten. The water produced in the body by oxidation was calculated from the amounts of carbohydrate, fat and protein in the daily diet which were estimated from the table of food analysis. In this calculation, the water produced from each 100 g. nutritive element was assumed to be 55.1 g. for carbohydrate, 107.1 g. for fat and 41.3 g. for protein (see Rowntree (17)). The water production thus calculated from the diet was 259 g. per day on the average.

To estimate the water output per day, the weights of daily urine and feces and the water loss from skin and lung were determined. The weight of urine and feces was calculated by subtracting the weight of their solid substances from the total weights of samples measured. The weight of solid substance of urine was calculated from Long's formula (16), while that of feces was obtained by measuring the dried feces.

The water loss from skin and lung (\(W\)) which is expressed in term of total perspiration and corresponds to the sum of insensible water loss and sweating was calculated from the difference of the body weights successively measured in two mornings \((m_1\) and \(m_2\)), the weight of diet daily taken \((D)\), the urine and feces weight \((E)\) and the weight loss by gaseous exchange \((G)\) as follows.

\[ W = (m_1 + D) - (m_2 + E + G) \]

The weight loss by gaseous exchange means the weight difference of CO\(_2\) expired from O\(_2\) inspired. To estimate this value, the daily energy consumption was determined by the time study of the subject's behaviors in the
laboratory, of which the energy consumptions per hour were measured previously by another experiment. The respiratory quotient in resting state was measured by Douglas bag method and, being assumed to be constant throughout the day, it was utilized in calculating the total CO$_2$ output and the total O$_2$ inhalation from the daily energy consumption. The difference of the weight of total CO$_2$ expired from that of total O$_2$ inspired corresponds $G$. By repeating determinations on the subjects, it was found that this value does not vary considerably on one and the same subject and lies from 183 to 223 g. per day among four subjects. Thus the value of each subject was assumed to be constant throughout the experiment.

The content of antidiuretic substance, ADS, in serum was determined by Birnie's method (18) to find a possible explanation of seasonal change of water metabolism. The principle of the method is as follows. The rats which belong to the same strain of Wister are fed for a week in the room of constant temperature of 22°C. prior to the experiment, and are divided into two groups, i.e. the one for the control experiment and the other for the test of serum ADS. After the rats being administered with a certain amount of water (24 cc/200 g. B.W. for 2 hours), 1 cc. serum per 200 g. B.W. is injected into the abdominal cavity of the test group, while the same amount of physiological saline to the control group. As the serum contains ADS, the excretion rate of urine of the test group was reduced as compared with that of the control group. Thus the content of ADS in serum can be estimated by the difference of the excretion rate of urine (% excretion of urine to water load in 90 minutes) between the two groups, and is designated Birnie unit. On details of the method, refer to the original paper (18).

**EXPERIMENTAL RESULTS**

I. Seasonal variations in the amount and distribution of water and salts of body fluid

A) Blood water and salts

Monthly alterations in serum specific gravity, serum water and protein content and hematocrit are shown in fig. 1, where the mean atmospheric temperature of each month and the mean room temperature at the time of blood sampling are also indicated. The specific gravity rises in winter and falls in summer. The change is accompanied with parallel changes in serum protein concentration and hematocrit, but with an opposite change in serum water content, as was reported by Kuroda (1). These facts clearly indicate that the dilution of blood and serum appears in summer and the concentration occurs in winter.

Fig. 2 shows seasonal variations in serum salt concentrations. Concentrations of Na, Cl and K in serum increase in winter, and decrease in summer. As these are the main salts in serum, the variations result in similar seasonal changes of osmotic pressure of serum which are represented by curves of the freezing point depression in the figure. All these changes are associated with the seasonal change of the atmospheric temperature, which was highest in July and lowest in January. It will be mentioned, however, that the month of
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FIG. 1. Seasonal variations of blood concentration.

FIG. 2. Seasonal variations of serum salt concentrations.

The maximum or the minimum value in the serum water and salts content does not coincide with that of the maximum or minimum temperature, but lags by one month or so, as is shown in figs. 1 and 2. This is probably because the change in blood composition is effected by an adaptative change of body fluid, which may lag behind the seasonal change of atmospheric temperature.

The annual means of water and salts concentrations in serum, as well as of other blood compositions and their averages in summer and winter are numerically presented in table 1. According to the custom in Japan, the average in summer was calculated from the values of June, July and August, while that in winter included the values of December, January and February. The differences between summer and winter averages were confirmed to be stochastically significant as indicated by asterisks in the table.

As is shown in the table, the serum protein concentration and the hematocrit decrease in summer and increase in winter by about 7% and 5.5% respectively. The serum Na and Cl concentrations present similar seasonal changes of 4.3% and 5.6% respectively, while K concentration shows a far
TABLE 1. Differences of Blood Compositions between Summer and Winter

<table>
<thead>
<tr>
<th></th>
<th>No. of Subj</th>
<th>Annual mean</th>
<th>Summer</th>
<th>Winter</th>
<th>Difference (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Specific gravity of serum</td>
<td>8</td>
<td>1.0254</td>
<td>1.0246</td>
<td>1.0262</td>
<td>-0.0016**</td>
</tr>
<tr>
<td>Water content of serum (%)</td>
<td>8</td>
<td>91.81</td>
<td>92.09</td>
<td>91.47</td>
<td>+0.62** (0.675%)</td>
</tr>
<tr>
<td>Serum protein concentration (g/dl)</td>
<td>4</td>
<td>7.09</td>
<td>6.87</td>
<td>7.37</td>
<td>-0.50** (-7.05%)</td>
</tr>
<tr>
<td>Freezing point depression of serum (°C)</td>
<td>4</td>
<td>0.561</td>
<td>0.529</td>
<td>0.581</td>
<td>-0.052** (-9.27%)</td>
</tr>
<tr>
<td>Serum Na concentration (mM/l)</td>
<td>8</td>
<td>143.5</td>
<td>140.8</td>
<td>146.9</td>
<td>-6.1*( -4.25%)</td>
</tr>
<tr>
<td>Serum Cl concentration (mM/l)</td>
<td>8</td>
<td>108.7</td>
<td>105.9</td>
<td>112.0</td>
<td>-6.1** (-5.61%)</td>
</tr>
<tr>
<td>Serum K concentration (mM/l)</td>
<td>8</td>
<td>3.93</td>
<td>3.44</td>
<td>4.43</td>
<td>-0.99** (-25.2%)</td>
</tr>
<tr>
<td>Serum Na/K ratio</td>
<td>8</td>
<td>38.2</td>
<td>43.1</td>
<td>34.3</td>
<td>+8.8** (23.04%)</td>
</tr>
<tr>
<td>Hematocrit (%)</td>
<td>8</td>
<td>42.2</td>
<td>41.4</td>
<td>43.7</td>
<td>-2.3** (-5.45%)</td>
</tr>
<tr>
<td>Total circulating blood volume per B.W. (cc/kg)</td>
<td>8</td>
<td>82.6</td>
<td>85.0</td>
<td>81.0</td>
<td>+4.0* (4.83%)</td>
</tr>
<tr>
<td>Total circulating serum volume per B.W. (cc/kg)</td>
<td>8</td>
<td>48.0</td>
<td>50.2</td>
<td>46.1</td>
<td>+4.1** (8.59%)</td>
</tr>
<tr>
<td>Total serum protein per B.W. (g/kg)</td>
<td>4</td>
<td>3.46</td>
<td>3.50</td>
<td>3.51</td>
<td>-0.01 (-0.25%)</td>
</tr>
<tr>
<td>Total serum Na per B.W. (mM/kg)</td>
<td>8</td>
<td>6.88</td>
<td>7.06</td>
<td>6.78</td>
<td>+0.38** (4.17%)</td>
</tr>
<tr>
<td>Total serum Cl per B.W. (mM/kg)</td>
<td>8</td>
<td>5.21</td>
<td>5.31</td>
<td>5.15</td>
<td>+0.16** (3.11%)</td>
</tr>
<tr>
<td>Total serum K per B.W. (mM/kg)</td>
<td>8</td>
<td>0.187</td>
<td>0.173</td>
<td>0.204</td>
<td>-0.031** (-16.6%)</td>
</tr>
<tr>
<td>Atmospheric temperature (°C)</td>
<td>15.5</td>
<td>25.7</td>
<td>25.9</td>
<td>19.7</td>
<td>+19.7</td>
</tr>
</tbody>
</table>

1) The value in summer represents the mean value of June, July and August, while that in winter is the mean value of December, January and February.
2) * means that the difference between summer and winter is significant at the level of 5% and ** indicates that at the level of 1%.
3) The difference is expressed as positive when the value in summer is higher than that in winter. The percentage of difference to the annual mean is given in parenthesis.
4) B.W. means the body weight in kg.

larger percentage change of about 25%. Thus the ratio of Na to K in serum increases in summer and decreases in winter (fig. 2).

To clarify the cause of these seasonal changes in blood compositions, the total circulating serum volume was measured monthly and the total amount of protein and salts and also the total blood volume were calculated. The results are shown in fig. 3 and in the lower half of table 1. The seasonal change in total circulating serum volume is so smooth that the change can never be attributed to experimental complications as was doubted by Bass and Henschel (8). The change of volume from winter to summer is by 8.6% of the annual mean 48.0 cc/kg. The absolute value in cc. of the change in total blood volume is the same as that of total serum volume, i.e. an increase of 4 cc/kg from winter to summer. It means that the seasonal change of circulating blood volume is mainly effected by the change of serum volume. These facts of hemodilution in hot climate coincide qualitatively with those reported by Barcroft and others ((2), (3), (4), (5)).

The total serum protein in circulating blood shows, however, no seasonal variation, as is seen in fig. 3 and also in table 1. The significance of the difference between winter and summer cannot be verified by Student’s test as well as by analysis of variance. The fact indicates that the dilution of serum
in summer is mainly effected by an increase of water amount in circulating serum.

As to the reason of the increase of serum water content, previous authors suggested an expansion of vascular bed in hot climate which initiates an inflow of tissue fluid into blood vessels. According to this hypothesis, the inflow of tissue fluid should be accompanied with the increase of chloride concentration in serum, because the chloride concentration in tissue fluid is higher than in serum by Donnan equilibrium. The experimental fact of chloride decrease in summer, however, contradicts this supposition. The change of Na/K ratio in serum cannot, also, be explained solely by this hypothesis. Thus seasonal changes of serum water and salts should be explained by taking another factor into consideration.

In an attempt to find some suggestion on this question, the total quantities of Na, Cl and K in circulating serum were calculated. As is shown in fig. 3 and table 1, the total Na and Cl contents are higher in summer than in winter by a rate of 3-4% of the annual mean, while the total K content is lower by 17%. The fact cannot be explained by a shift of tissue fluid in blood, but strongly suggests the presence of seasonal changes in water and salts metabolisms which may cause changes in amount and distribution of water and salts in body fluid.

B) Volumes of body fluid compartments

To ascertain the above assumption, the volumes of total body water (TBW),
FIG. 4. Seasonal variations of body fluid distribution and of salt contents in extracellular fluid (per body weight).

summer and winter is, however, about the same as that of ICF, as the absolute amount of the latter is larger than the former. The variation of TBW corresponds to the mean of the two. These seasonal alterations in body fluid compartments are stochastically significant. With regard to the ratios of ECF/TBW and of ICF/TBW, seasonal variations cannot be verified to be significant, though ECF/TBW tends to increase in summer, while ECF/TBW decreases. From these, it seems certain that the seasonal variation of water metabolism may cause primarily the change of extracellular compartment, which results secondly in changes of intracellular fluid and finally in total body fluid.

Seasonal variations in body fluid compartments were already observed by Forbes, Dill and Hall (7) who found decrease of thiocyanate space in hot
TABLE 2. Seasonal Variations of Body Fluid Distribution and Salt Contents in Extracellular Fluid

<table>
<thead>
<tr>
<th></th>
<th>No. of Subj.</th>
<th>Annual mean</th>
<th>Summer</th>
<th>Winter</th>
<th>Difference (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body weight (kg.)</td>
<td>4</td>
<td>52.04</td>
<td>52.50</td>
<td>51.89</td>
<td>+0.61(1.2%)</td>
</tr>
<tr>
<td>Total body water/B.W. (%)</td>
<td>4</td>
<td>60.4</td>
<td>63.3</td>
<td>56.8</td>
<td>+6.5**(10.8%)</td>
</tr>
<tr>
<td>Extracellular fluid/B.W. (%)</td>
<td>4</td>
<td>22.4</td>
<td>23.7</td>
<td>20.6</td>
<td>+3.1**(13.8%)</td>
</tr>
<tr>
<td>Intracellular fluid/B.W. (%)</td>
<td>4</td>
<td>38.0</td>
<td>39.7</td>
<td>36.2</td>
<td>+3.5**(9.2%)</td>
</tr>
<tr>
<td>ECF/TBW (%)</td>
<td>4</td>
<td>37.1</td>
<td>37.4</td>
<td>36.3</td>
<td>+1.1(3.0%)</td>
</tr>
<tr>
<td>ICF/TBW (%)</td>
<td>4</td>
<td>62.9</td>
<td>62.6</td>
<td>63.7</td>
<td>-1.1(-1.8%)</td>
</tr>
<tr>
<td>Total Na in ECF/B.W. (mM/kg.)</td>
<td>4</td>
<td>29.53</td>
<td>30.8</td>
<td>27.9</td>
<td>+2.9**(9.8%)</td>
</tr>
<tr>
<td>Total Cl in ECF/B.W. (mM/kg.)</td>
<td>4</td>
<td>24.90</td>
<td>25.9</td>
<td>23.0</td>
<td>+2.9**(11.8%)</td>
</tr>
<tr>
<td>Total K in ECF/B.W. (mM/kg.)</td>
<td>4</td>
<td>0.938</td>
<td>0.897</td>
<td>0.969</td>
<td>-0.072(*)(-7.7%)</td>
</tr>
</tbody>
</table>

1) The value in summer represents the mean value of June, July, and August, while that in winter is the mean value of December, January, and February.
2) TBW is the total body water, ECF the extracellular fluid, ICF the intracellular fluid, and TSW the total serum water.
3) The other symbols are the same with those in table 1.
4) The seasonal difference is subjected to analysis of variance and the statistical significance is indicated by asterisk, i.e. * is significant on 5% level and ** on 1% level. (*) means higher but very closely near 5% level.

In short, the author verified that the body fluid compartments present seasonal variations which probably reflect on similar variations of circulating serum as well as blood volumes.

C) Salts of extracellular fluid

From the extracellular fluid volume and salts concentrations of serum, the total salts content of extracellular fluid, S, were calculated by following formulae,

For Na and K: \[ S = 0.95 \times P \times ECF, \]
For Cl: \[ S = 1.05 \times P \times ECF, \]

where \( P \) is a salt concentration in serum water. Concentrations of salts being expressed in mEq/l., and body fluid compartments in l. per kg. of body weight (B.W.), the total salts contents thus calculated are shown in fig. 4 and table 2. Na and Cl contents in ECF increase in summer and decrease in winter, while the seasonal change of K in ECF is reversed i.e. decrease in summer and increase in winter. All these seasonal changes are qualitatively the same as those in total salts contents in circulating serum and are stochastically significant as are shown in table 2.

In short, the salt contents in ECF show seasonal variations of which directions are different among salts. To explain these varieties of seasonal
changes, it is necessary to take salt metabolism into consideration as it may be specific to each salt.

**II. Seasonal variations of water metabolism and of ADS content in serum**

To verify the assumption described in the previous section, the water metabolism of four subjects were determined daily for a week in each of four seasons. Results are illustrated in fig. 5, where the mean value of experimental week of each subject is expressed with a line, and the mean of the four subjects in each season is represented by a broad column.

As is shown in the figure, the total water intake increases in summer and decreases in winter. The difference corresponds to 27% of the annual mean of daily intake (2,694 cc/day). This variation is verified to be stochastically significant by Student's test at the level of 1%. The daily water elimination also shows seasonal variations which appear in the total perspiration and the urinary output in the figure. The total perspiration there presented includes insensible water loss and sweating. It increases in hot season and decreases in cold season. The seasonal difference is stochastically significant at the level of 1%. On the other hand, the daily urine excretion increases in winter and decreases in summer. The urine output of autumn in the figure is pretty high as compared with that of winter. This is probably due to an exceptionally high water intake in autumn experiment occurring accidentally. This effect of large water intake disappears, however, by calculating the percentage ratio of urine excretion to the total water intake, and thus the ratio shows a gradual change from winter to summer. The daily water balance is closely near zero as is shown in the figure. The null hypothesis of this value cannot be denied by Fisher's test. The total water output varies therefore in direct proportion to changes in water intake.

In order to elucidate the mechanism of seasonal change of water metabolism, the content of ADS in serum was measured. As can be seen from fig. 5, it increases in summer and decreases

![FIG. 5. Seasonal variations of water metabolism and serum ADS content](image)
in winter. The seasonal difference is significant at the level of 1%. As ADS accelerates reabsorption of water from the kidney and reduces the urine volume, this seasonal variation may play the most important role in the decrease of urinary output in summer which was previously explained by an increase of sweating.

As a cause of the seasonal variation of ADS in serum, a seasonal change in secretion of antidiuretic hormone, ADH, from the pituitary gland may be considered most probable. In the measurement of ADS in serum, the sample was taken at the basal condition in the morning, and the subjects were neither subjected to dehydration nor to hydration at that time. Therefore this seasonal change in ADH secretion may be a result of seasonal change in secretory function of the endocrine gland. This problem will be discussed later in connection with seasonal adaptation of water metabolism.

DISCUSSION

In the above experiments, it was clarified that the amount and distribution of body fluid and salts show seasonal variations and these changes seem to be initiated by some adaptative mechanism to change of climate. Discussions will be performed on reasons and significances of these seasonal variations in body fluids.

Effects of alterations in water metabolism on seasonal change in body fluid volume should first be mentioned. The increase in water metabolism in summer causes to augment the extracellular fluid volume and in turn results in an increase of intracellular fluid and finally that of total body fluid. This increase of extracellular fluid volume also reflects in the increase of circulating serum volume and thus the blood is diluted in summer. In winter, the reverse change occurs and causes reduction of body fluid compartments and hemoconcentration.

As to the reason why the metabolic change of water changes the body fluid amount, the seasonal change of ADS content in serum may be regarded as the most important factor. Its increase in summer creates a tendency to conserve water in the body, especially in extracellular fluid by accelerating the reabsorption of water from kidney. On the other hand, the decrease of ADS in winter accelerates the urinary excretion and thus may reduce the body fluid amount.

For the reason of seasonal change of ADS content in serum, effects of climatic change should primarily be concerned. Since the atmospheric temperature rises in summer, the perspiration increases considerably and results in increase of total water elimination which causes a tendency to dehydration. The dehydration stimulates the osmoregulatory centre in hypothalamus and causes thirst sensation which initiates an increase in water intake. Another effect of the dehydration is an acceleration of secretion of ADH from pituitary gland which acts to conserve water from being excreted as urine. Moreover, it may be assumed that exposure to heat acts on the pituitary gland to secrete ADH by some neural mechanism (21). In any way, water balance may be maintained by such central mechanisms when water elimination is increased in
hot climate. Since these central apparatus, *i.e.* the osmoregulatory centre and pituitary gland, are supposed to be stimulated frequently in summer, some adaptative change may very probably occur in their activities. Thus the ADS content in serum may be raised and the hydrated state may always be maintained in summer by increasing the amount of body fluid on the one hand, and by decreasing the osmotic pressure of extracellular fluid on the other hand.

The reduction of ADS in serum as well as the decrease of water intake in winter may be explained by the mechanism reverse to that mentioned above.

Some evidences of this hypothesis on seasonal changes in regulation of water metabolism are cited as follows. Itoh (21) verified that when rats were exposed to heat (air temperature of 33-40° C.) for one hour or two, the secretion of ADH from the posterior lobe of pituitary gland was increased, while it was inhibited in those exposed to cold. He suggested some neural mechanisms by heat and cold to explain these facts. The ADH production in the hypothalamic region to cover its release from the pituitary gland was also verified to be enhanced in summer and reduced in winter.

In the present experiment, it was shown that the osmotic pressure of serum decreases in summer and increases in winter. If the activity of osmoregulatory centre in hypothalamus is kept constant throughout the year, such an seasonal alteration of serum osmotic pressure should not exist. Therefore, it is reasonable to postulate the seasonal variation in activity of osmoregulatory centre. As was mentioned above, the increased secretory activity of pituitary posterior lobe may create a tendency of hydration in summer, to which the osmoregulatory centre should adapt, and regulate the osmotic pressure at a somewhat lower level than in winter. The situation may be reversed in winter. These are reasons why the hydrated state is maintained in summer relative to in winter.

In summer, sweating is considerably increased by hot climate, and the body fluid is always threatened to be dehydrated. The hydration actually maintained by adaptative change of water metabolism may be regarded as a preparatory state of counter action to this threat.

Reasons of seasonal changes of salts contents in extracellular fluid will be discussed as the second problem. Since the volume of extracellular fluid increases in summer and decreases in winter, the total salt contents should change similarly, if the osmotic pressure were controlled to be constant. Actually however, the osmotic pressure presented a seasonal variation. Moreover the ratio of Na/K also presents a seasonal variation. Therefore, the seasonal change of salt contents cannot be explained as a secondary effect of body fluid change, but its main reason may lie in seasonal changes in salt metabolism. The fact that the seasonal change of Na in extracellular fluid is reverse to that of K strongly suggests seasonal alterations in activity of mineral corticoid from adrenal cortex, *i.e.* an increase of its secretion in summer and a decrease in winter.

There are many evidences that Na is accumulated while K is depleted in extracellular fluid by mineral corticoid, *e.g.* DCA, aldosterone, etc. (Gaunt (22) Yoshimura et al. (23)). Few have, however, been discussed about seasonal variations of production or secretion of mineral corticoid, though some suggestive
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facts can be enumerated. For example, Conn (24) verified that adrenocortical hormone can reduce Na/K ratio in sweat and according to Kuno (25), Cl and probably Na concentrations in sweat are lowered in summer than in winter.

These seasonal changes of salt metabolism seem to have important physiological significances. The increase of NaCl content in the extracellular fluid in summer may play a rôle in preventing salt deficiency by copious sweating. As K concentration of extracellular fluid may influence excitabilities of muscle and nerve, and metabolism of glucose (26), its increase in winter may play a rôle in maintaining activities of muscle and nerve in cold and high level metabolism which are favorable to establish adaptative changes of thermo-regulative functions in winter. In this connection, it may be interesting to cite Ogawa's report (27) in which the serum K concentration of tropical natives is ascertained to be lower than that of Japanese.

In short, seasonal changes of water and salts metabolism and of water and salt contents in body fluids, especially in ECF, seem to play important rôles in establishment of adaptation to seasonal change of climate.

SUMMARY

Seasonal alterations of distribution and amount of water and salts were studied on adult male subjects at basal condition and following results were obtained.

1) The serum water content increases in summer and decreases in winter, while the serum protein concentration and the hematocrit present reverse changes.

2) The total circulating serum volume as well as the blood volume also undergo the same course of seasonal changes. The serum volume is higher in summer than in winter by 8.6% of the annual mean, and the change of blood volume is mainly effected by that of serum volume.

3) As the total circulating serum protein is maintained almost constant throughout the year, the above mentioned seasonal changes are mainly due to hemodilution in summer and hemoconcentration in winter by changes of water content in circulating serum.

4) The total body water (TBW), the extracellular fluid (ECF) and the intracellular fluid (ICF), all increase in summer and decrease in winter. The percentage change of ECF is the most remarkable among the others, while the absolute amount of ICF change approximately coincides with that of ECF change, because ICF is far higher in its absolute volume than ECF. The seasonal change of water amount in circulating serum seems to be mainly effected by the change of ECF.

5) The water metabolism, including the intake of water and its elimination from the body, increases in summer and decreases in winter and thus the water balance is maintained at zero level in each season after the acclimatization has been attained. Seasonal change of total water output is mainly due to that of the total perspiration (insensible water loss + sweating), which undergoes a similar change, while the urinary output changes reversely.
6) The ADS content in serum increases in summer and decreases in winter, while the level of osmotic pressure in serum presents a reverse change. From these, it is presumed that the central regulatory mechanism of water metabolism, including the functions of the osmoregulatory centre and pituitary gland, is put in function to conform to seasonal change of water elimination, especially of perspiration.

7) Seasonal variations of serum water, ECF, ICF and TBW can be explained by this postulation of climatic adaptation of water metabolism. The seasonal variation of urinary excretion can also be explained by this change of central control of water metabolism, i.e. change of water reabsorption from kidney due to seasonal change of ADH secretion.

8) Na, Cl and K concentrations in serum show also seasonal variations, decreasing in summer and increasing in winter. The change of K concentration is far larger than the other two, and thus the ratio of Na/K increases in summer while it decreases in winter.

9) The total Na and Cl contents in circulating serum and as well as in ECF increase in summer and decrease in winter, while the total K content in both compartments changes reversely. From these, it is suggested that secretion of mineral corticoid may undergo a seasonal variation.

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